EMA/627978/2021

# European Medicines Agency decision

P/0507/2021

of 3 December 2021

on the acceptance of a modification of an agreed paediatric investigation plan for pretomanid, (EMEA-002115-PIP01-17-M04) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

**Disclaimer**

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

**Only the English text is authentic.**

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0058/2019 issued on 26 February 2019, the decision P/0337/2019 issued on 10 September 2019 and the decision P/0340/2020 issued on 9 September 2020,

Having regard to the application submitted by Global Alliance for TB Drug Development on 8 July 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 October 2021, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

***Article 1***

Changes to the agreed paediatric investigation plan for pretomanid, tablet, dispersible tablet, oral use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

***Article 2***

This decision is addressed to Global Alliance for TB Drug Development, 40 Wall Street, NY 10005 - New York, United States.

EMA/PDCO/405053/2021
Amsterdam, 15 October 2021

# Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-002115-PIP01-17-M04

## Scope of the application

**Active substance(s):**

Pretomanid

**Condition(s):**

Treatment of multi-drug-resistant tuberculosis

**Pharmaceutical form(s):**

Tablet

Dispersible tablet

**Route(s) of administration:**

Oral use

**Name/corporate name of the PIP applicant:**

Global Alliance for TB Drug Development

## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Global Alliance for TB Drug Development submitted to the European Medicines Agency on 8 July 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0058/2019 issued on 26 February 2019, the decision P/0337/2019 issued on 10 September 2019 and the decision P/0340/2020 issued on 9 September 2020.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 17 August 2021.

## Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

## Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

# Annex I

# The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

# 1. Waiver

Not applicable.

# 2. Paediatric investigation plan

## *2.1. Condition:*

Treatment of multi-drug-resistant tuberculosis

### 2.1.1. Indication(s) targeted by the PIP

Pretomanid is indicated for use as part of an appropriate combination regimen for pulmonary multi-drug resistant tuberculosis (MDR-TB) when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability.

### 2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age.

### 2.1.3. Pharmaceutical form(s)

Tablet

Dispersible tablet

### 2.1.4. Measures

| Area | Number of measures | Description |
|---|---|---|
| Quality-related studies | 1 | **Study 1**<br>Development of dispersible tablet formulation. |
| Non-clinical studies | 1 | **Study 2**<br>Juvenile toxicity study in rats. |
| Clinical studies | 3 | **Study 3 (BA-Study)**<br>An open-label, randomized, 4-period crossover study in 2 panels of healthy, adult subjects to assess the relative bioavailability, food effect, and dose dependence of the formulations of pretomanid.<br>**Study 4 (PAEDIATRIC-1)**<br>An open-label, single-dose study to assess the pharmacokinetics, safety and tolerability of pretomanid in paediatric patients with rifampin-resistant (RR) tuberculosis (TB). |

| | | |
|---|---|---|
| | | **Study 5 (PAEDIATRIC-2)**<br><br>An open-label, multicenter study to evaluate the pharmacokinetics, safety, tolerability and anti-mycobacterial activity of pretomanid in combination with bedaquiline and linezolid (B-Pa-L) for the treatment of paediatric patients with confirmed or probable pulmonary pre-extensively-resistant or extensively drug-resistant tuberculosis (pre-XDR/XDR-TB), or those who have failed or are intolerant to treatment for multidrug-resistant tuberculosis (MDR-TB). |
| Extrapolation, modelling and simulation studies | 2 | **Study 6**<br><br>Population pharmacokinetic (PK) modelling and simulation study in paediatric patients with pulmonary (with or without extrapulmonary) infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).<br><br>**Study 7**<br><br>Extrapolation study of the clinical efficacy and safety data for pretomanid in combination with bedaquiline and linezolid (B-Pa-L regimen) from adult patients to paediatrics patients with pulmonary (with or without extrapulmonary) infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB). |
| Other studies | 0 | Not applicable. |
| Other measures | 0 | Not applicable. |

# 3. Follow-up, completion and deferral of PIP

| | |
|---|---|
| Concerns on potential long term safety/efficacy issues in relation to paediatric use: | Yes |
| Date of completion of the paediatric investigation plan: | By June 2025 |
| Deferral for one or more measures contained in the paediatric investigation plan: | Yes |